THE ROLE OF LIPID EMULSION IN ORGANOPHOSPHORUS PESTICIDE POISONING IN CLINICAL PRACTICE

Simeonka Dimitrova, Gabriela Kehayova, Petko Marinov

Department of Pharmacology, Toxicology and Pharmacotherapy, Faculty of Pharmacy, Medical University of Varna

ABSTRACT

INTRODUCTION: A major clinical and important for the public health issue causing many deaths is acute organophosphorus pesticide (OP) poisoning. The clinical behaviour during these cases of intoxication has improved slightly in recent years, but the same two antidotes are still used—atropine and oximes, as well as the standard resuscitation and detoxification methods. There are many experiments and clinical cases that demonstrate the benefit of lipid emulsions (LEs) in cases of intoxication with lipophilic agents, as well as with pesticides.

CASE PRESENTATION: A retrospective study has been performed on 20 patients with cases of acute exogenous pesticide intoxication. An intravenous LE was administered to four of them as an add-on therapy to the main therapeutic regimen.

RESULTS: A quantitative assessment of consciousness was made—the majority of patients entered the hospital in a severe condition, the state of consciousness of 3 patients receiving LE (75%) was defined as obnubilation and one patient (25%) was in a coma. In LE-free control cases, the most common complications were exotoxic shock (37.5%), acute respiratory failure (31.25%), and arterial hypotension (31.25%). In the patient control group, the mortality was 50% (8 cases), and in those treated with LE, 1 patient died (25% of cases).

CONCLUSION: Based on these clinical data, we believe that lipid emulsion can be useful in the treatment of intoxication with acute exogenous pesticides as an add-on to antidote therapy.

Keywords: *atropine, cardiac and respiratory failure, coma, lipid emulsions, mechanical ventilation, organophosphorus compounds, poisoning*

Address for correspondence:
Simeonka Dimitrova
Faculty of Pharmacy
Medical University of Varna
84 Tzar Osvoboditel Blvd
9002 Varna
e-mail: monikdd@abv.bg

Received: November 15, 2019
Accepted: December 8, 2019

INTRODUCTION

Acute exogenous pesticide intoxications are characterized with a relatively high mortality rate of about 20-30% and a severe course of the disease (1). Organophosphorus (OP) compounds inhibit acetylcholinesterase activity, which triggers acetylcholine accumulation in synapses and causes acetylcholine receptors to overstimulate in the autonomic and cen-

tral nervous systems, as well as in the neuromuscular synapse. This disrupts the neurotransmission in these structures.

The main symptoms of intoxication include: vomiting, bradycardia, hypotension, tears, increased sweating, hypersalivation, abnormal coordination, slurred speech, loss of reflexes, muscle weakness, bronchospasm, and incontinence (2). Patients are hospitalized with a Glasgow Consciousness Scale (GCS) assessment since it provides the best prognosis for the outcome of intoxication—the risk of death for patients with GCS 15/15 is <5%, while the risk of death for patients with GCS <10/15 is 60%. GCS is a clear result marker for poisoning with OPs (3). Irrespective of the mode of exposure, several causes of the severe course and adverse outcome of intoxication are usually identified in patients with acute toxic effects, and these are cardiac or respiratory failure (4). Therefore, the two main elements of the clinical management of acute intoxication with dimethoate are maintenance of the respiratory tract and administration of antidotes. Severe toxicity results in acute respiratory failure caused by paralysis of the respiratory muscles, neuromuscular dysfunction and bronchorrhea. Patients require resuscitation; administration of oxygen, infusion solutions, atropine as an antidote and mechanical ventilation (5). Prompt treatment is key to prevent complications and fatalities in acute poisoning with OPs. Most authors recommend gastric lavage with single doses of activated charcoal within one hour of intoxication, if the patient is conscious. Atropine is the most important antidote for poisoning with OPs and it is also effective in carbamate poisoning (4). It is given intravenously to quickly restore adequate cardiorespiratory function—a process often called "atropinisation". It is used to treat bradycardia and improve systolic blood pressure, to reduce bronchorrhea and bronchospasm.

CASE PRESENTATION

Retrospective study has been performed on 20 patients with cases of acute exogenous pesticide intoxication. An intravenous lipid emulsion (LE) was administered to four of them as an add-on therapy to the main therapeutic regimen.

Two of the cases of pesticide poisoning (50%) treated at the Military Medical Academy–Varna for the period 2010-2020 with LE, were given dimethoate, the rest—1 received phenytrothione (25%) and 1—a combination of cypermethrin and chlorpyrifos ethyl (25%). LE was administered as a bolus dose of 1.5 mL/kg followed by an intravenous infusion at a rate of 0.25 mL/kg/min.

RESULTS

Clinical symptoms of intoxication occurred within hours of exposure to pesticides and patients arrived within 24 hours after intoxication.

The majority of patients entered the hospital in a severe condition—the state of consciousness of 3 patients receiving LE (75%) was defined as obnubilation and one patient (25%) was in a coma. In the LE-free control group, two patients (12.5%) had obnubilation, one patient had sopor (6.25%), 6 (37.5%) were in a coma, and 7 (43.75%) had no changes in consciousness (Fig. 1). As an expression of the main toxic mechanism of OPs, the plasma cholinesterase activity was decreased, and in the group of patients with lipid resuscitation it was significantly lower than in the control group (P<0.001).

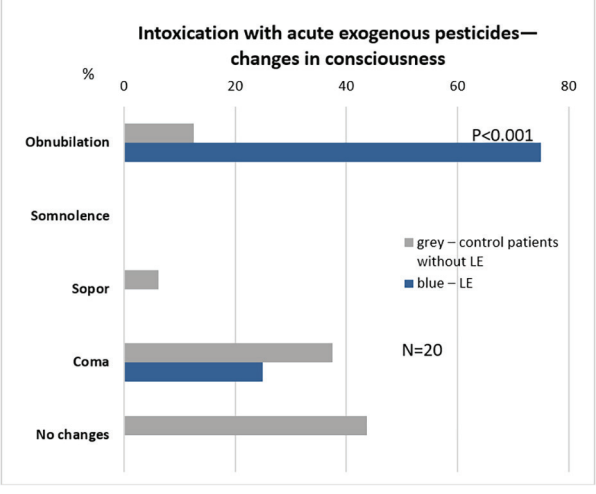


Fig. 1. Changes in consciousness during pesticide intoxication at the admission of the patients

The characteristic symptoms of intoxication—changes in muscle tone and motor activity—were evident in both groups. One patient in each group had paraesthesias and two in each group had depressed muscle tone. Hypersalivation and incontinence occurred in the LE group twice as frequently as in the control group (Fig. 2).

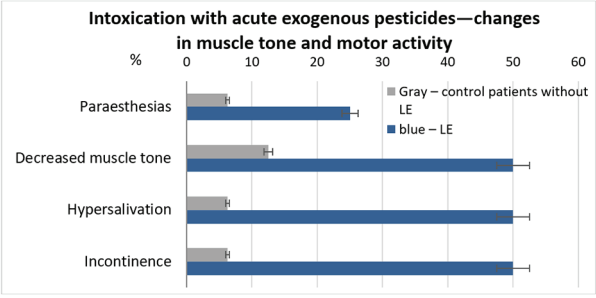
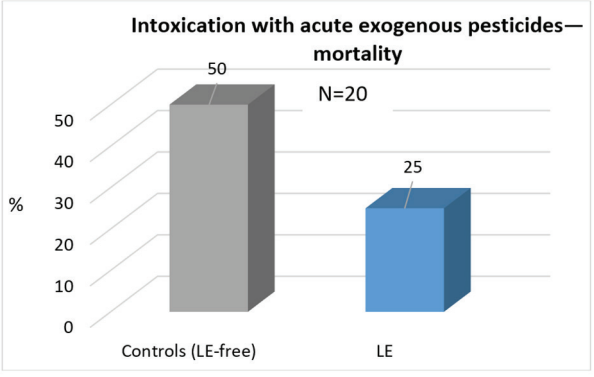


Fig. 2. Symptoms of intoxication—changes in muscle tone and motor activity

The most common complications in the LE-free control cases were exotoxic shock (37.5%), acute respiratory failure (31.25%), and arterial hypotension (31.25%). The group was dominated by concomitant diseases of the cardiovascular system, there were patients with pulmonary diseases and diabetes mellitus (Fig. 3). In cases of acute pesticide poisoning with LE, the following complications were observed—pulmonary oedema in two patients, sinus tachycardia and arterial hypertension in three (75%), toxic myocarditis in two, toxic polyneuritis and polyneuropathy in one patient, and one developed toxic hepatitis. The data correlate with the clinical laboratory parameters of the intoxicated patients, namely a reliably increased GGT activity, 20% higher ALT activity com-



gray—control patients without LE; blue—LE

Fig. 4. Mortality in cases of pesticide intoxication

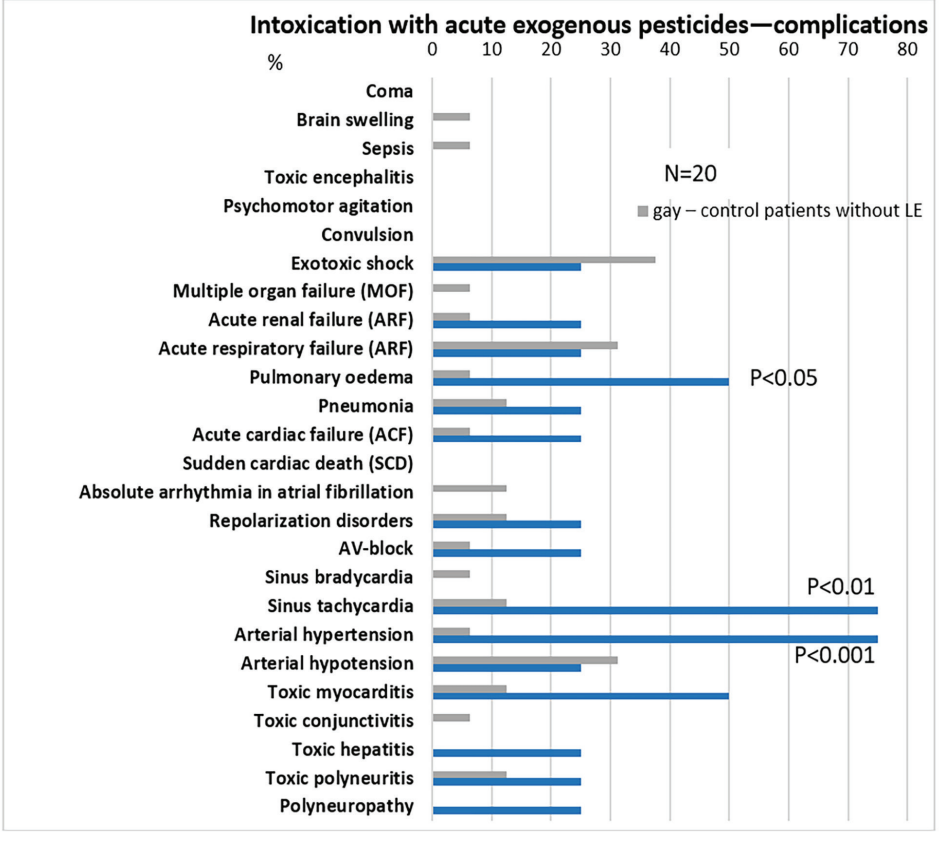


Fig. 3. Complications during pesticide intoxication therapy

pared to controls, and increased blood glucose levels (by 20%).

Cases of pesticide intoxication are extremely risky with a high lethality rate despite the application of adequate and timely treatment. The benefit of LE in cases of pesticide intoxication is also evident from mortality reporting. In the patient control group, the mortality was 50% (8 cases), and in those treated with LE, 1 patient died (25% of cases) (Fig. 4).

CONCLUSION

Based on these clinical data, we believe that lipid emulsion can be useful in the treatment of intoxication with acute exogenous pesticides as an add-on to antidote therapy.

REFERENCES

1. Ke X, Zhi S, Zheng D, Hong G, Zhag G, Li M, et al. Analyses on relevant factors of the prognosis of patients with acute organophosphate poisoning. Zhonghua Lao Dong Wel Sheng Zhi Ye Bing Za Zhi. 2015;33(3):186-9.
2. Lotti M. Clinical toxicology of anticholinesterase agents in humans. In: Krieger R, editor. Handbook of pesticide toxicology. 2 ed. Vol. 2. San Diego: Academic Press; 2001. pp. 1043–85.
3. Davies JO, Eddleston M, Buckley NA. Predicting outcome in acute organophosphorus poisoning with a poison severity score or the Glasgow coma scale. QJM. 2008;101(5):371-9. doi: 10.1093/qjmed/hcn014.
4. Eddlestone M. Pattern and problems of deliberate self-poisoning in the developing world. QJM. 2000;93(11):715–31. doi: 10.1093/qjmed/93.11.715.
5. Eddleston M, Buckley NA, Eyer P, Dawson AH. Medical management of acute organophosphorus pesticide poisoning. Lancet. 2008; 371(9612):597–607. doi: 10.1016/S0140-6736(07)61202-1.